UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/742,454 | 12/19/2000 | Steven R. Wiley | 2968-B | 8855 |

22932 7590 07/02/2002

IMMUNEX CORPORATION
LAW DEPARTMENT
51 UNIVERSITY STREET
SEATTLE, WA 98101

| EXAMINER | |
|---|---|
| YAEN, CHRISTOPHER H | |
| ART UNIT | PAPER NUMBER |
| 1642 | 11 |

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/742,454 | Applicant(s) WILEY, STEVEN R. | |
|---|---|---|---|
| | Examiner Christopher H Yaen | Art Unit 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,6-23 and 39* is/are pending in the application.

4a) Of the above claim(s) *7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,8-23 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6-8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. The examiner of the application has changed. This case has now been transferred as of 6/20/02. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Christopher Yaen, Group Art Unit 1642.

### *Election/Restrictions*

2. Upon further reconsideration, claim 39 will be **rejoined** into group I. Applicant's amendments (paper no. 10) have been entered. Claim 7 is withdrawn from consideration, as being drawn to a non-elected species. Claims 1-3, 6, 8-23 and 39 are considered on the merits.

### *Information Disclosure Statement*

3. The Information Disclosure Statements filed 5/14/01, 6/25/01, and 10/15/01 (Papers Nos: 6-8) are acknowledged. A signed copy is attached hereto.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3,6,8-23, and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. In regards to claims 1, 8, 9 and dependent claims thereof, in the recitation of the term *"variant"* and *"fragment"*, it is unclear and indefinite. The specification fails to

indicate what the terms encompass. Absent such a disclosure, the metes and bounds of the claimed invention cannot be determined and thus renders the claims indefinite.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1,6,8,11,12, and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting angiogenesis comprising the adminstration of an antagonist comprising an Fc polypeptide fusion protein comprising amino acids 28-79 of SEQ ID No: 7 and an antibody directed at TWEAK receptor, does not reasonably provide enablement for a method of modulating angiogenesis through the administration of any antibody, fragment, variant or antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and practice the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276

(CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

*The nature of the invention:* The claimed invention is drawn to a method of modulating angiogenesis through the administration of an antagonist to the TWEAK receptor, wherein the receptor antagonist comprises an antibody, an Fc-polypeptide fusion, and variants/fragments. The antagonist, antibody, and variants/fragments of claims 1, 6,8,11,and 12 encompasses virtually any antagonist, antibody, and variants/fragments to that may act as an antagonist to the TWEAK receptor.

*The state of the prior art and the predictability or lack thereof in the art:* The art teaches TWEAK and the TWEAK receptor, as it relates to apoptosis and as an inducer of angiogenesis (Lynch *et al* J. Biol. Chem. 1999;274(13):8455-8459, IDS). Furthermore, the art teaches of TWEAK as having *"potency similar to bFGF and VEGF",* as a potential stimulator of angiogenesis. However, the art fails to disclose or describe any antagonists that are capable of modulating angiogenesis. It also fails to establish with

any certainty that an antagonist to the TWEAK receptor is a potential agent for such modulation.

*The amount of direction or guidance present and the presence or absence of working examples:* The specification discloses the use of an Fc-polypeptide fusion construct and antibodies that are capable of inhibiting angiogenesis. Furthermore, the specification discloses the use of these molecules antagonizing the binding of TWEAK to its receptor. The specification, however, does not teach how to make and use the antagonists as they related to enhancing angiogenesis. Nor does the specification teach or disclose of any specific variants/fragments, antibodies, or any agonist other than an antagonist comprising an Fc-polypeptide fusion construct (wherein the polypeptide portion consists of 28-79). All the examples of the instant specification are directed to the description creation of, the use of, and the effects of an antagonist (Fc-polypeptide), on angiogenesis.

*The breadth of the claims and the quantity of experimentation needed:* Given the broad range of method of modulating through the administration of antagonists, antibodies, and variants/fragments within the claims; the absence of any specific teachings in the specification with regards to antagonists, antibodies, and variants/fragments; and the lack of any prior art that would indicate that the administration of the claimed invention could modulate angiogenesis, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

9. Claims 1-3, 6, 8-23, and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth amino acids set forth in SEQ ID No: 7, therefore the written description is not commensurate in scope with the claims which read on naturally occurring variants and fragments.

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

What are allelic variants? Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites ( page 17). Thus, the structure of naturally occurring allelic sequences are not defined, nor in this case, is the structure of allelic variant proteins encoded by allelic variant genes defined. With the exception of SEQ ID NO:7, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and or encoded variants and therefore conception is not achieved until reduction to practice has

occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

Furthermore, although drawn specifically drawn to the DNA art the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for allelic variants is provided in the specification on page 7 lines 25-35, where it is disclosed that "A TWEAKR protein refers to a protein that retains the ability to bind the ligand." However, no disclosure, beyond the mere mention of allelic variants is made in the specification. This is insufficient to support the generic claims as

provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an Fc-polypeptide molecule having an amino acid sequence shown in SEQ ID NO. 7 meets the written description provision of 35 USC 112, first paragraph.

***Conclusion***

No claim is allowed. Claims 1-3,6,8-23, and 39 are free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
June 28, 2002

Brenda Brumback
BRENDA BRUMBACK
~~PATENT~~ EXAMINER
PRIMARY